

**What is claimed is:**

1) A method of predicting pharmacologic and/or pharmacokinetic and/or pharmacodynamic activity of a test material comprising the steps of:

incubating different concentrations of the test material with cell and/or protozoa and/or micro-organism; and determining the change in the morphology of the cell and/or protozoa and/or micro-organism;

wherein said change in the morphology serves for the calculation of the effective concentration of the test material in the blood, thereby predicting pharmacologic and/or pharmacokinetic and/or pharmacodynamic activity of the test material.

2) A method of predicting the effective concentration of a test material in the blood comprising the steps of:

incubating different concentrations of the test material with cell and/or protozoa and/or micro-organism; and determining the change in the morphology of the cell and/or protozoa and/or micro-organism;

wherein said change in the morphology serve for the calculation of the effective concentration of the test material in the blood, thereby predicting the effective concentration of the test material.

3) A method of predicting the plateau/maximum/steady state/peak concentration of a test material in the blood comprising the steps of:

incubating different concentrations of the test material with cell and/or protozoa and/or micro-organism; and determining the change in the morphology of the cell and/or protozoa and/or micro-organism;

wherein change in the morphology serve for the calculation of the effective concentration of the test material in the blood, thereby predicting the plateau/maximum/steady state/peak concentration of the test material.

4) A method of selecting a composition among a plurality of compositions, which comprise the same active ingredient, so as to obtain an effective concentration of the active ingredient in the blood, comprising the steps of:

incubating at least one dose of each composition with cell and/or protozoa and/or micro-organism; determining the change in the morphology of the cell and/or protozoa and/or micro-organism; so as to select a composition, which is capable of providing an effective concentration of the active ingredient in the blood, thereby selecting a composition among a plurality of compositions, which comprise the same

active ingredient, so as to obtain an effective concentration of the active ingredient in the blood.

5) A method of selecting a composition among a plurality of compositions, which comprise the same active ingredient, so as to obtain plateau/maximum/steady state/peak concentration of the active ingredient in the blood, comprising the steps of: incubating at least one dose of each composition with cell and/or protozoa and/or micro-organism; determining the change in the morphology of the cell and/or protozoa and/or micro-organism; so as to select a composition, which is capable of providing an effective concentration of the active ingredient in the blood, thereby selecting a composition among a plurality of compositions, which comprise the same active ingredient, so as to obtain an effective concentration of the active ingredient in the blood.

6. A method of predicting the effective concentration of a drug in the blood comprising the steps of: incubating different concentrations of the drug with Tetrahymena species and/or other cultured cells; determining the difference in the proliferation rate of the Tetrahymena species and/or other cultured cells; wherein said proliferative effect serve for the calculation of the effective concentration of the test material in the blood, thereby predicting the effective concentration of a drug.

7. A method of selecting a composition among a plurality of compositions, which comprise the same active ingredient, so as to obtain an effective concentration of the active ingredient in the blood, comprising the steps of: incubating at least one dose of each composition with Tetrahymena species and/or other cultured cells; determining the difference in the proliferation of the Tetrahymena species and/or other cultured cells, and comparing said difference elicited by each composition, wherein a composition which causes higher difference in proliferation will have higher concentration of the active ingredient in the blood; thereby selecting a composition among a plurality of compositions, which comprise the same active ingredient, so as to obtain an effective concentration of the active ingredient in the blood.

8. The method of Claims 1-5, wherein said change in morphology is a change in area, shape factor, volume, radius, perimeter or the diameter of cell and/or protozoa and/or micro-organism.

9. The method of Claims 1-7, wherein said protozoa is from the group of *Tetrahymena pyriformis* or *Tetrahymena thermophila*, *Tetrahymena Borealis*, *Tetrahymena Americanis*.
10. The method of Claims 1-9, wherein said change in morphology is a change in area, shape factor, volume, radius, perimeter or the diameter of the cell and/or protozoa and/or micro-organisms.
11. The method of Claims 1-10, wherein said change in morphology is evaluated by image analysis, computerized image analysis, morphometric program or morphometric bioassay.
12. A method according to Claim 1, wherein the pharmacologic and/or pharmacokinetic and/or pharmacodynamic activity is toxicity and/or metabolism and/or distribution and/or elimination and combination thereof.
13. The method of Claims 1-10 wherein the test material is a drug, a lead compound or a chemical entity.
14. The method of Claim 1, further comprising a step of comparing the morphological effect on the cell and/or protozoa and/or micro-organism and the pharmacological effect of at least two known drugs of the family of drugs to which the test material belong to, so as to predict the pharmacological effect of the test material.
15. The method of Claims 2-13, further comprising a step of comparing the morphological effect on the cell and/or protozoa and/or micro-organism and the pharmacological effect of at least two known drugs of the family of drugs to which the test material belong to, so as to predict the blood concentration of the test material.
16. A method according to claims 1-13 to be used for predicting test material concentration in blood, plasma, serum, extracellular fluid or lymph.
17. An apparatus comprising a) a donor compartment for retaining a sample of test material to be tested for extent of diffusion and/or permeation through a test membrane; and (b) a receiver compartment, which comprises cells and/or protozoa and/or microorganisms, wherein said test membrane is located between said donor compartment and said receiver compartment.

18. The apparatus of claim 17, wherein said receiver compartment comprises any species of the groups of *Tetrahymena pyriformis* or *Tetrahymena thermophila*, *Tetrahymena Borealis*, *Tetrahymena Americanis*.
19. The apparatus of claim 17, wherein said test membrane is a biphasic membrane possessing hydrophobic and hydrophilic layers.
20. The apparatus according to claims 17-19, wherein said test membrane is from natural, synthetic or semi-synthetic source.
21. The apparatus according to claims 17-20, wherein said test membrane is animal tissue, human tissue, plant tissue, cultured collagen on silicone membrane.
22. A apparatus according to claim 23, wherein the biphasic is composed of silastic/silicone and collagen.
23. A apparatus according to claim 20, wherein the hydrophobic layer is comprised of silicone.
24. A apparatus according to claim 20, wherein the hydrophobic layer is comprised of collagen and glycosaminoglycan.
25. A apparatus according to claim 20, wherein the hydrophobic layer is comprised of silicone and the hydrophobic layer is comprised of collagen and glycosaminoglycan.
26. A apparatus according to claim 20, wherein a hydrophilic layer is comprised of at least one of the following components: collagen, elastin, fibrin, cell culture, synthetic hydrophilic materials, hydrophilic polymers, glycosaminoglycan, proteins or combination thereof.
27. A apparatus according to claim 20, wherein the hydrophobic layer is comprised of a one of the following components: silastic, silicone, ceramides, cholesterol, cholesteryl esters, cholesterol derivatives, phospholipids, free fatty acids, ~~esters~~ of free fatty acids, cellulose acetate/nitrate membrane, pure cellulose acetate with/without wetting agent, polysulfone membrane, glass fiber, Teflon, or combination thereof.
28. A apparatus according to claims 17-29, wherein the thickness of the hydrophilic part is 0.005-3mm.

29. A apparatus according to claims 17-29, wherein the thickness of the lypophylic layer is 0.005-1mm.
30. A apparatus according to claims 17-29, wherein the thickness of the hydrophilic part is 0.05-3mm.
31. A apparatus according to claims 17-29, wherein the thickness of the lypophylic layer is 0.005-0.25mm.
32. An apparatus according to claims 20-33 in the form sacks and/or "teabags" and/or tubes and/or pockets and/or plates, dishes and/or containers.
33. A system comprising at least one apparatus according to any one of the claims 20-33.
34. A system according to claim 34 wherein the apparatus are shared and/or separated.
35. A method of predicting pharmacologic and/or pharmacokinetic and/or pharmacodynamic activity of a test material comprising the steps of:  
administering to the donor compartment according to claims 17-35, a sample of the test material and determining the difference in the morphology caused by the test material, on said cells and/or protozoa and/or micro-organisms, wherein said morphological difference serves for the predicting pharmacologic and/or pharmacokinetic and/or pharmacodynamic activity.
- 36) A method of predicting the effective concentration of a test material in the blood comprising the steps of:  
administering to the donor compartment according to claims 17-35, a sample of the test material; and determining the change in the morphology of said cell and/or protozoa and/or micro-organism;  
wherein change in the morphology serve for the calculation of the effective concentration of the test material in the blood, thereby predicting the effective concentration of test material.
37. A method of predicting the sub-minimum, plateau/maximum/steady state/peak concentration of a test material in the blood comprising the steps of:  
administering to the donor compartment according to claims 17-35, a sample of the test material; and determining the change in the morphology of said cell and/or protozoa and/or micro-organism;

wherein change in the morphology serve for the calculation of the effective concentration of the test material in the blood, thereby predicting the sub-minimum, plateau/maximum/steady state/peak concentration of test material.

38. A method of selecting a dermal or transdermal or cosmetic composition among a plurality of compositions, which comprise the same active ingredient, so as to obtain an effective concentration of the active ingredient in the blood, comprising the steps of:

adding at least one dose of each composition to the apparatus of claim 17-36; determining the change in the morphology of the cell and/or protozoa and/or micro-organism; so as to select a composition, which is capable of providing an effective concentration of the active ingredient in the blood, thereby selecting a composition among a plurality of compositions, which comprise the same active ingredient, so as to obtain an effective concentration of the active ingredient in the blood.

39. A method of selecting a dermal or transdermal or cosmetic compound among a plurality of compounds, so as to obtain an effective concentration of the active ingredient in the blood, comprising the steps of:

adding at least one dose of each compound to the apparatus of claim 17-35; determining the difference in the morphology of the cell and/or protozoa and/or micro-organism; so as to select a composition, which is capable of providing an effective concentration of the active ingredient in the blood, thereby selecting a composition among a plurality of compositions, which comprise the same active ingredient, so as to obtain an effective concentration of the active ingredient in the blood.

40. A method of predicting the effective concentration of a drug in the blood comprising the steps of: adding at least one dose of each compound to the apparatus of claim 17-36; and determining the difference in the proliferation rate of said cell and/or protozoa and/or micro-organism; wherein said proliferative rate serves for the calculation of the effective concentration of the test material in the blood, thereby predicting the effective concentration of a drug.

41. A method of selecting a composition among a plurality of compositions, which comprise the same active ingredient, so as to obtain an effective concentration of the active ingredient in the blood, comprising the steps of: adding at least one dose of each composition to the apparatus of claims 17-35; determining the difference in the proliferation of said cell and/or protozoa and/or micro-organism so as to select a

composition, which is capable of providing an effective concentration of the active ingredient in the blood, thereby selecting a composition among a plurality of compositions, which comprise the same active ingredient, so as to obtain an effective concentration of the active ingredient in the blood.

42. The method of Claims 37-40, wherein said change in morphology is a change in area, shape factor, volume, radius, perimeter or the diameter of cell and/or protozoa and/or micro-organism .

43. The method of Claims 37-42, wherein said protozoa is any species of the groups of *Tetrahymena pyriformis* or *Tetrahymena thermophila*, *Tetrahymena Borealis*, *Tetrahymena Americanis*.

44. The method of Claims 37-40, wherein said change in morphology is a change in area, shape factor, volume, radius, perimeter or the diameter of the cell and or protozoa and or micro-organisms.

45. The method of Claims 37-41, wherein said change in morphology is evaluated by image analysis, computerized image analysis, morphometric program or morphometric bioassay.

46. A method according to Claim 37, wherein the pharmacologic and/or pharmacokinetic and/or pharmacodynamic activity is toxicity and/or metabolism and/or distribution and/or elimination and combination thereof.

47. The method of Claims 37-43, wherein the test material is a drug, a lead compound or a chemical entity.

48. The method of Claims 37, further comprising a step of comparing the morphological effect on the cell/protozoa or micro-organism and the pharmacological effect of at least two known drugs of the family of drugs to which the test material belong to, so as to predict the pharmacological effect of the test material.

49. The method of Claims 38-40, further comprising a step of comparing the morphological effect on the cell/protozoa or micro-organism and the pharmacological effect of at least two known drugs of the family of drugs to which the test material belong to, so as to predict the blood concentration of the test material.

50. A method according to claims 37-40 to be used for predicting test material concentration in blood, plasma, serum, extracellular fluid or lymph.
51. A method according to the claims 37-40 said protozoa is any species of the groups of *Tetrahymena pyriformis* or *Tetrahymena thermophila*, *Tetrahymena Borealis*, *Tetrahymena Americanis*.
52. Use of an a bi-phasic membrane comprising of silicon or silicate and collagen for measuring permeation or diffusion of a test material through a membrane.
53. The use of claim 52, wherein said test membrane is a biphasic membrane possessing hydrophobic and hydrophilic layers.
54. The use according to claim 52, wherein said test membrane is from natural, synthetic or semi-synthetic source.
55. The use according to claim 52, wherein said membrane is animal tissue, human tissue, plant tissue, cultured collagen on silicone membrane.
56. Use according to claim 53, wherein the hydrophobic layer is comprised of silicone or silicate.
57. Use according to claim 53, wherein the hydrophobic layer is comprised of collagen and glycosamynoglycan.
58. Use according to claim 53, wherein the hydrophobic layer is comprised of silicone and the hydrophobic layer is comprised of collagen and glycosamynoglycan.
59. Use according to claim 53, wherein a hydrophilic layer is comprised of at least one of the additional components: elastin, fibrin, cell culture, synthetic hydrophilic materials, hydrophilic polymers, glycosamynoglycan, proteins or combination thereof.
60. Use according to claim 53, wherein the hydrophobic layer is comprised of a one of the following components: silastic, silicone, ceramides, cholesterol, cholesteryl esters, cholesterol derivatives, phospholipids, free fatty acids, esters of free fatty acids, cellulose acetate/nitrate membrane, pure cellulose acetate with/without wetting agent, polysulfone membrane, glass fiber, Teflon, or combination thereof.
61. Use according to claim 53, wherein the thickness of the hydrophilic part is 0.005-3mm.



62. Use according to claim 53, wherein the thickness of the lypophylic layer is 0.005-1mm.
63. Use according to claim 53, wherein the thickness of the hydrophilic part is 0.05-3mm.
64. Use according to claim 54, wherein the thickness of the lypophylic layer is 0.005-0.25mm.
65. Use of a membrane according to claim 52 for selecting a transdermal composition among a plurality of compositions, which comprise the same active ingredient.
66. Use of a membrane according to claim 52 for selecting a transdermal compound among a plurality of compounds.
67. Use according to claim 52 for selecting a dermal composition among a plurality of compositions, which comprise the same active ingredient.
68. Use according to claim 52 for selecting a dermal compound among a plurality of compounds.
69. Use according to claim 52 for selecting a dermal composition among a plurality of compositions, which comprise the same active ingredient.
70. Use according to claim 52 for selecting a dermal compound among a plurality of compounds.